



General

Guideline Title

Guidelines for the evaluation and management of status epilepticus.

Bibliographic Source(s)

Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, Laroche SM, Riviello JJ Jr, Shutter L, Sperling MR, Treiman DM, Vespa PM, Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care*. 2012 Aug;17(1):3-23. [246 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions of the strength of recommendations (*strong, weak*) and quality of the evidence (*high, moderate, low, very low*) are provided at the end of the "Major Recommendations" field.

Status Epilepticus (SE) Definition and Classification Recommendations

1. SE should be defined as 5 min or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures (*strong recommendation, moderate quality*).
2. SE should be classified as either convulsive SE (convulsions that are associated with rhythmic jerking of the extremities) or non-convulsive SE (seizure activity seen on electroencephalogram [EEG] without the clinical findings associated with convulsive SE) (*strong recommendation, high quality*).
3. Refractory SE should be defined as SE that does not respond to the standard treatment regimens, such as an initial benzodiazepine followed by another antiepileptic drug (AED) (*strong recommendation, moderate quality*).
4. The etiology of SE should be diagnosed and treated as soon as possible (*strong recommendation, high quality*).

Treatment Recommendations

The treatment of SE should include the appropriate elements of critical care as outlined in Table 5 in the original guideline document. Also see Table 6 in the original guideline document for specific recommendations emergent, urgent, and refractory treatment.

1. The treatment of convulsive SE should occur rapidly and continue sequentially until clinical seizures are halted (*strong recommendation, high quality*).

2. The treatment of SE should occur rapidly and continue sequentially until electrographic seizures are halted (*strong recommendation, moderate quality*).
3. Critical care treatment and monitoring should be started simultaneously with emergent initial therapy and continued until further therapy is considered successful or futile (*strong recommendation, moderate quality*).
4. Treatment options
 - a. Benzodiazepines should be given as emergent initial therapy (*strong recommendation, high quality*).
 - i. Lorazepam is the drug of choice for intravenous (IV) administration (*strong recommendation, moderate quality*).
 - ii. Midazolam is the drug of choice for intramuscular (IM) administration (*strong recommendation, moderate quality*).
 - iii. Rectal diazepam can be given when there is no IV access and IM administration of midazolam is contraindicated (*strong recommendation, moderate quality*).
 - b. Urgent control AED therapy recommendations include use of IV fosphenytoin/phenytoin, valproate sodium, or levetiracetam (*strong recommendation, moderate quality*).
 - c. Refractory SE therapy recommendations should consist of continuous infusion AEDs, but vary by the patient's underlying condition (*strong recommendation, low quality*).
 - d. Dosing of continuous infusion AEDs for refractory status epilepticus (RSE) should be titrated to cessation of electrographic seizures or burst suppression (*strong recommendation, very low quality*).
 - e. A period of 24–48 h of electrographic control is recommended prior to slow withdrawal of continuous infusion AEDs for RSE (*weak recommendation, very low quality*).
 - f. During the transition from continuous infusion AEDs in RSE, it is suggested to use maintenance AEDs and monitor for recurrent seizures by continuous electroencephalogram (cEEG) during the titration period. If the patient is being treated for RSE at a facility without cEEG capabilities, consider transfer to a facility that can offer cEEG monitoring (*strong recommendation, very low quality*).
 - g. Alternative therapies can be considered if cessation of seizures cannot be achieved; however, it is recommended to reserve these therapies for patients who do not respond to RSE AED treatment and consider transfer of the patient if they are not being managed by an intensive care unit (ICU) team that specializes in the treatment of SE and/or cannot provide cEEG monitoring (*weak recommendation, very low quality*).

Continuous Electroencephalogram (cEEG) Recommendations

The indications for cEEG are outlined in Table 10 in the original guideline document, and cEEG defined treatment endpoints are outlined in Table 11 in the original guideline document.

1. The use of cEEG is usually required for the treatment of SE (*strong recommendation, very low quality*).
2. Continuous EEG monitoring should be initiated within 1 hour of SE onset if ongoing seizures are suspected (*strong recommendation, low quality*).
3. The duration of cEEG monitoring should be at least 48 hours in comatose patients to evaluate for non-convulsive seizures (*strong recommendation, low quality*).
4. The person reading EEG in the ICU setting should have specialized training in cEEG interpretation, including the ability to analyze raw EEG as well as quantitative EEG tracings (*strong recommendation, low quality*).

Definitions:

Strength of Recommendations

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system offers two grades of recommendations: strong and weak. One advantage of the GRADE system is that a strong recommendation can be made using weak to moderate evidence based on these four factors:

1. Balance between desirable and undesirable effects if the effect is very desirable, a stronger recommendation is given.
2. Quality of evidence (see definitions below for high, moderate, low, and very low quality evidence).
3. Values and preferences—if the values and preferences are similar, or there is greater certainty in them, then a stronger recommendation is given.
4. Costs (resource allocation)—lower costs of an intervention (e.g., the fewer the resources consumed) are linked to a higher likelihood that a strong recommendation is warranted.

Quality of Evidence

High Quality - Further research is very unlikely to change confidence in the estimate of effect

Moderate Quality - Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate

Low Quality - Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate

Very Low Quality - Any estimate of effect is very uncertain

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Status epilepticus (convulsive, non-convulsive and refractory)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Critical Care

Emergency Medicine

Internal Medicine

Neurology

Pediatrics

Intended Users

Advanced Practice Nurses

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To address evaluation and management of status epilepticus (SE) in critically ill adults and children

- To describe SE definitions and classification, etiology, diagnostic evaluation, prognosis, treatment, monitoring, and future directions

Target Population

Critically ill adults and children with suspected or confirmed status epilepticus

Note: The guideline does not address treatment in neonates.

Interventions and Practices Considered

Diagnosis/Evaluation

1. Classifying status epilepticus (SE) as convulsive or non-convulsive based on clinical and electroencephalogram (EEG) findings
2. Defining refractory SE based on response to standard treatment
3. Diagnosing the etiology of SE

Treatment/Management

1. Rapid and sequential treatment of convulsive SE
2. Critical care treatment and monitoring
3. Treatment
 - Benzodiazepines as emergent initial treatment
 - Urgent control antiepileptic drug (AED) therapy (intravenous [IV] fosphenytoin/phenytoin, valproate sodium, or levetiracetam)
 - Refractory SE therapy using continuous infusion of AED
 - Titrated dosing of continuous infusion AEDs for refractory status epilepticus (RSE) based on cessation of electrographic seizures or burst suppression
 - Slow withdrawal of continuous infusion AEDs for RSE
 - Use of maintenance AEDs and monitoring for recurrent seizures by continuous EEG (cEEG) during the titration period
 - Use of alternative therapies in nonresponding patients
4. Use of cEEG monitoring during treatment, with reading by persons with specialized training

Major Outcomes Considered

- Mortality and morbidity associated with status epilepticus (SE)
- Cessation of clinical and electrographic seizure activity due to SE
- Maintenance of control of SE
- Adverse effects of treatment

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

A PubMed/Medline literature search was performed for relevant articles published through August 2011, using the following search terms: status epilepticus, refractory seizures, and nonconvulsive status epilepticus plus individual seizure treatments, including standard medications and other

anticonvulsive therapies (e.g., cooling and ketogenic diet). The search was limited to articles describing human subjects that were published in the English language. Clinical trials, meta-analyses, review articles, and practice guidelines were all eligible for inclusion. Studies describing treatment were limited to those that included at least 5 patients. Results were supplemented with literature recommended by the committee or identified from reference lists.

Many management decisions lack prospective randomized controlled trials upon which static epilepticus (SE) treatment recommendations can be based. Therefore, the writing committee also presented data from previously published surveys and a survey of an international panel of experts specifically conducted for the development of these guidelines. In addition, citations to several important review articles outside of the specified search criteria were included at the recommendation of external reviewers.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Diagnosis and Management Recommendations

Quality of Evidence Based on Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)

High Quality - Further research is very unlikely to change confidence in the estimate of effect

Moderate Quality - Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate

Low Quality - Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate

Very Low Quality - Any estimate of effect is very uncertain

See Table 1 in the original guideline document for the evidence rating system based on American Heart Association/American College of Cardiology guidelines.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Articles selected for inclusion in the treatment recommendations underwent a review by the writing committee. Treatment recommendations were then assigned a level of evidence based on the American Heart Association statement and guideline development (see Table 1 in the original guideline document). Diagnosis and management of status epilepticus were assigned a recommendation based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. See the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields for definitions.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Neurocritical Care Society Status Epilepticus Guideline Writing Committee was established in 2008 to develop evidence-based expert consensus guidelines for diagnosing and managing static epilepticus (SE). Co-chairs were selected by the Neurocritical Care Society, with ten additional neurointensivists and epileptologists from across the United States included on the committee. After the committee prepared an initial set of guidelines based on literature review and committee consensus, recommendations were reviewed by a group of external experts in SE management, whose comments were incorporated into the final document.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system offers two grades of recommendations: strong and weak. One advantage of the GRADE system is that a strong recommendation can be made using weak to moderate evidence based on these four factors:

1. Balance between desirable and undesirable effects if the effect is very desirable, a stronger recommendation is given.
2. Quality of evidence (see the "Rating Scheme for the Strength of the Evidence" field for definitions).
3. Values and preferences—if the values and preferences are similar, or there is greater certainty in them, then a stronger recommendation is given.
4. Costs (resource allocation)—lower costs of an intervention (e.g., the fewer the resources consumed) are linked to a higher likelihood that a strong recommendation is warranted.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

After the Neurocritical Care Society Status Epilepticus (SE) Guideline Writing Committee prepared an initial set of guidelines based on literature review and committee consensus, recommendations were reviewed by a group of external experts in SE management, whose comments were incorporated into the final document.

All participants agreed with the recommendations presented in this guideline.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Rapid seizure control and maintenance of seizure control
- Reduced patient morbidity and mortality through appropriate acute treatment, monitoring, and management of status epilepticus (SE)

Potential Harms

- Infusions with phenytoin and fosphenytoin should occur with cardiac monitoring, due to increased risk for QT prolongation and arrhythmias.
- Valproate sodium should be used with caution in patients with traumatic head injury.
- Tachyphylaxis occurs after prolonged use of midazolam.
- Other side effects of medications such as:
 - Neurotoxicity
 - Hypotension
 - Cardiopulmonary depression
 - Metabolic acidosis
 - Withdrawal seizures
 - Birth defects from antiepileptic drugs (AEDs)
 - Propofol infusion syndrome
 - Hepatotoxicity when using valproate in younger children

Refer to Tables 7 and 8 in the original guideline for drug-specific information concerning serious adverse effects and cautions for use of anti-epileptic drugs.

Contraindications

Contraindications

Propofol is contraindicated in young children.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, Laroche SM, Riviello JJ Jr, Shutter L, Sperling MR, Treiman DM, Vespa PM, Neurocritical Care Society Status Epilepticus Guideline Writing Committee. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care*. 2012 Aug;17(1):3-23. [246 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Apr 24

Guideline Developer(s)

Neurocritical Care Society - Medical Specialty Society

Source(s) of Funding

Neurocritical Care Society

Guideline Committee

Neurocritical Care Society Status Epilepticus Guideline Writing Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [Neurocritical Care Society Web site](#) .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 3, 2012. The information was verified by the guideline developer on August 15, 2012. This summary was updated by ECRI Institute on July 10, 2013 following the U.S. Food and Drug Administration advisory on Valproate.

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